15 | Family History of Heart Disease

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Definition

A family history of heart disease is obtained to identify the presence of cardiovascular disease or genetically determined disorders in the family that may affect the cardiovascular system of the patient or his or her descendants.

Technique

The following approach provides a detailed pedigree that applies to all possible inherited illnesses. The patient is asked to list all family members, living and dead, beginning with the oldest child and proceeding through each of the children, brothers, sisters, parents, uncles, aunts, and grandparents. Parental consanguinity (parents who are blood relatives) should be elicited, since this will significantly increase the possibility of a rare, recessively inherited disease. The name, age, sex, location, state of health, and occurrence of congenital defects or significant illnesses should be obtained. The race, religious, and ethnic background and the occurrence of abortions, stillbirths, miscarriages, and early death are important. Other family members may also provide more detailed knowledge about the family ancestors and relatives.

A possible family history of cardiovascular disease should be specifically explored by phrasing questions in several ways to avoid overlooking important information. The following areas should be emphasized:

1. Family members with known heart or vascular disease. This should include myocardial infarction (heart attack, coronary thrombosis), heart failure (congestion, dropsy), aneurysm (bubble, blowout of artery), stroke (CVA, hardening of arteries), sudden death, arrhythmia (rhythm disturbance, WPW, irregular or racing heart), and rheumatic fever.
2. Familial risk factors for cardiovascular disease. These include hypertension (high blood pressure, high blood), diabetes mellitus (high sugar), and hyperlipidemia (high fat, high cholesterol).
3. Congenital heart disease or a genetic syndrome in the family. The questions should focus on birth defects, a blue baby, unusual stature, and mental or physical retardation. The possibility of maternal rubella, drugs, alcohol, and viral infections during pregnancy should be questioned.

Basic Science

Cardiovascular disorders with a proven or suggested familial basis include congenital heart disease, atherosclerotic heart disease, hypertension, and rheumatic heart disease

The studies by Nora and Nora (1978a) of a large number of patients with congenital heart disease showed that about 8% of the defects were primarily related to genetic factors, 2% were environmental, and 90% were multifactorial. The environmental catalysts included drugs, viruses, maternal nutrition, maternal metabolism, or fetal hemodynamics. Specific cardiovascular teratogens included drugs such as alcohol (associated with ventricular septal defect, VSD, patent ductus arteriosus, PDA, and atrial septal defect, ASD), amphetamines (VSD, PDA, ASD, transposition of the great arteries, TGA), the anticonvulsants hydantoin (pulmonic stenosis, PS, aortic stenosis, AS, PDA, coarctation of aorta) and trimethadione (TGA, tetralogy of Fallot, hypoplastic left heart), lithium (Ebstein anomaly, tricuspid atresia, ASD), sex hormones (VSD, TGA, tetralogy), thalidomide (tetralogy, VSD, ASD, truncus arteriosus), and disease states such as rubella (peripheral pulmonary artery stenosis, PDA, VSD, ASD), diabetes (TGA, VSD, coarctation of aorta), lupus erythematosus (heart block), and phenylketonuria (tetralogy, VSD, ASD). The multifactorial group is thought to consist of patients with a genetic predisposition to cardiovascular disease due to small, additive effects of many genes (polygenic) and an environmental trigger that produces a cardiovascular malformation. The Noras (1978a) concluded that "the production of an anomaly by a teratogen requires certain conditions including: genetic predisposition to maldevelopment, genetic predisposition to react adversely to the teratogen, and exposure to the teratogen at the vulnerable period of embryonic development."

This study and others have noted that the recurrence risk for congenital cardiovascular disease in families increases two- to threefold when there are two affected family members, particularly when the two affected first-degree relatives are parent and child or when the patient is severely affected. The more common the prevalence of the defect in the general population, the more likely it is to recur in first-degree relatives. A history of parental consanguinity is especially important; second cousins have a 1 in 32 chance of sharing a particular gene, whereas third cousins have a 1 in 128 likelihood. Once the family history establishes that a disorder is inherited through a Mendelian pattern, the likelihood that the patient is similarly affected can be estimated.

A family history of coronary disease has been elusive to define as an *independent* risk factor because multiple risk factors—diabetes, cigarette smoking, hyperlipidemia, and hypertension—also cluster in families. Multivariate analysis has indicated that a history of myocardial infarction in a first-degree relative confers a risk two to three times that of a person without a family history. This is particularly important for coronary disease presenting before late middle age and in patients who have a minimum risk profile otherwise. Familial hyperlipidemia and hypertension are strong risk factors in predicting the development of coronary disease in family members.

Table 15.1
Genetic Diseases of the Cardiovascular System[a]

Genetic diseases associated with an abnormal electrocardiogram or arrhythmia
- Adrenogenital syndrome (AR-20170)
- Conduction defects (AD-11390, 11508)
- Friedreich's ataxia (AR-22930)
- Leopard syndrome (AD-15110)
- Mitral valve prolapse (AD-15770)
- Muscular dystrophy (X-31020)
- Myotonic dystrophy (AD-16090)
- Ocular myopathy (AD-16510)
- Periodic paralysis (AD-17040)
- Prolonged Q-T interval (AD-22040)
- Refsum's disease (AR-26650)
- Wolff-Parkinson-White syndrome (AD-19420)

Genetic diseases that affect the myocardium
- Amyloidosis (AD-10500)
- Cardiomyopathy (AD-19260)
- Friedreich's ataxia (AR-22930)
- Glycogen storage disease (AR-23230)
- Hemochromatosis (AD-14160)
- Hypertrophic subaortic stenosis (AD-19260)
- Leopard syndrome (AD-15110)
- Muscular dystrophy (X-31020)
- Myotonic dystrophy (AD-16090)
- Noonan's syndrome (AD-16395)
- Refsum's disease (AR-26650)
- Sickle cell disease (AD-14170)
- Thalassemia major (AR-27350)
- Tuberous sclerosis (AD-19110)

Genetic diseases affecting the pericardium
- Mulibrey nanism (AR-25325)

Genetic diseases affecting valves or septa
- Alcaptonuria (AR-20350)
- Aortic stenosis, supravalvular (AD-18550)
- Apert's syndrome (AD-10120)
- Atrial septal defect (AD-108880, AR-20940)
- Carpenter's syndrome (AR-20100)
- Chondrodysplasia punctata (AR-21510)
- Chromosomal aberrations
  - Trisomy 8 mosaic
  - Trisomy 9 mosaic
  - Trisomy 13
  - Trisomy 18
  - Trisomy 21
  - Trisomy 22
  - Trisomy 22, partial
  - 4 p—
  - 5 p—
  - 13 q—
  - +14 q—
  - 18 q—
- Delange syndrome (AD-12247)
- Ebstein's anomaly (AR-22470)
- Ehlers–Danlos syndrome (AD-13000)
- Ellis–Van Creveld syndrome (AR-22550)
- Fanconi's pancytopenia (AR-22765)

Genetic diseases affecting valves or septa *(continued)*
- Forney syndrome (AD-not listed)
- Holt-Oram syndrome (AD-14290)
- Klippel–Feil syndrome (AD-14890)
- Laurence-Moon-Biedl-Bardet syndrome (AR-24580)
- Leopard syndrome (AD-15110)
- Marfan's syndrome (AD-15470)
- Mitral valve prolapse (AD-15770)
- Mucopolysaccharidosis (AR-25280)
- Noonan's syndrome (AD-16395)
- Osteogenesis imperfecta (AD-16620)
- Patent ductus arteriosus (AD-16910)
- Pierre–Robin syndrome (AR-26180)
- Pseudoxanthoma elasticum (AR & AD-17860)
- Pulmonic stenosis (AR-26550)
- Rubinstein–Taybi syndrome (AR-26860)
- Silver syndrome (AR-27005)
- Smith-Lemli-Opitz syndrome (AR-27040)
- Thrombocytopenia—absent radius (AR-27400)
- Treacher-Collins syndrome (AD-15440)
- Turner's syndrome
- Weill-Marchesani syndrome (AR-27760)
- XXXXY (C)
- Zellweger's syndrome (AR-21410)

Genetic diseases that affect the vascular system
- Anomalous pulmonary venous return (AD-10670)
- Apert's syndrome (AD-10120)
- Arterial tortuosity (AR-20805)
- Coarctation of the aorta (AD-12000)
- Cockayne syndrome (AR-21640)
- Coronary atherosclerosis (U)
- Crouzon syndrome (AD-12350)
- Cutis laxis (AD-12370 & AR-21910)
- Diabetes mellitus (U)
- Ehlers-Danlos syndrome (AD-13000)
- Erdheim's cystic medial necrosis (AD-13290)
- Fabry's disease (X-30150)
- Goldenhar syndrome (AR-25770)
- Hemorrhagic telangiectasia (AD-18730)
- Homocystinuria (AR-23620)
- Hyperlipidemia (AD-14425)
- Hypertension, essential (U-14550)
- Hypotension, orthostatic (AD-14650)
- Klippel–Trenaunay–Weber syndrome (AD-14900)
- Menkes' syndrome (X-30940)
- Mucopolysaccharidosis (AR-25280)
- Marfan's syndrome (AD-15470)
- Neurofibromatosis (AD-16220)
- Osler–Weber–Rendu syndrome (AD-18730)
- Osteogenesis imperfecta (AD-16620)
- Progeria (AR-26410)
- Pseudoxanthoma elasticum (AR & AD-17785)
- Pulmonary hypertension, primary (AD-17860)
- Turner's syndrome (C)
- Varicose veins (AD-19220)
- Von Hippel–Lindau disease (AD-19330)
- Werner's syndrome (AR-27770)
- XXXXY (C)

[a]Based on McKusick (4). See that source for descriptions of the disorders and further references.

AS = aortic stenosis; ASD = atrial septal defect; PDA = patent ductus arteriosus; PS = pulmonic stenosis; Tetralogy = tetralogy of Fallot; TGA = transposition of the great arteries; Truncus = truncus arteriosus; VSD = ventricular septal defect; AD = autosomal dominant; AR = autosomal recessive; X = sex linked; C = chromosomal; U = uncertain.

A family history of hypertension is twice as common in the hypertensive population as in normotensives. A polygenic mode of inheritance has been found. Genetic factors include an inherited defect in cellular sodium transport as well as abnormal response to psychogenic stress. Pheochromocytoma is a rare cause of hypertension that may be familial.

A high familial incidence of rheumatic fever has been reported; however, the genetic influence does not follow a Mendelian pattern, and environmental factors may play an interacting role.

Clinical Significance

Inherited cardiovascular diseases may involve only the cardiovascular system or be a component of a more extensive genetic disorder such as Down's syndrome. The possibility of a genetically determined disease may be immediately apparent, as in the Ellis–Van Creveld syndrome, or be only an indirect, poorly understood influence, as in coronary atherosclerosis. Some forms of heart disease, such as mitral valve prolapse or atrial septal defect, may be genetically determined in some patients but not in others. The importance of a family history is emphasized by the number and variety of problems that can be transmitted by Mendelian inheritance, multifactorial influences, or chromosomal abnormalities. An extensive although incomplete list would include genetic diseases associated with an abnormal electrocardiogram or arrhythmia and diseases affecting the myocardium, the pericardium, the valves and septa, or the vascular system generally. In Table 15.1, the number following the disease refers to the citation in McKusick (1983), where a brief description of the problem and several additional references can be located.

References

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